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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,084	09/06/2000	Barry N. Kreiswirth	19124.0002	8869

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EXAMINER	
ZEMAN, MARY K	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/656,084	KREISWIRTH ET AL.	
	Examiner	Art Unit	
	Mary K. Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,8,10-14,16,17,21-36,38 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7,8,10-14,16,17,21-36,38 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/12/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In view of the arguments filed on 11/28/05, PROSECUTION IS HEREBY REOPENED. New Grounds of Rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Ardin Marschel, SPE 1631.

Ardin H Marschel 3/10/06
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER

The pending claims are 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38 and 44.

Claims 42-43 stand withdrawn from consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 1/12/06 was filed after the mailing date of the appeal brief on 11/28/05. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32, 33, 34-36 38 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 32, the metes and bounds of the system claiming a remote facility are unclear. How does a contained system comprise something that is remote? What are the metes and bounds of "remote"? At what point is a facility considered to be remote? From what is it remote- the computer? How does a facility take samples from a patient? It would appear that individuals or health care workers *within* a facility would take the samples, and not the remote facility itself, and not the claimed system. A system is an interlinked set of physical elements such as a computer, display and output; or article of manufacture and controller.

Similarly, the metes and bounds of the term "remote" in claims 34 -36 are unclear. At what point is the facility remote from where the sequencing is performed? On a different table? In a different room? In a different building?

The metes and bounds of the software code of claim 33 are unclear. How does a software code obtain samples from a patient? Software code cannot physically obtain a sample. Further, software code cannot sequence a sample.

It is unclear how the limitation of claim 44 further limits the system of claim 32. Where in the system does the sequencing occur? What is required to perform the sequencing? A hardware element? A software element? A scientist?

The metes and bounds of claim 38 are entirely unclear. How can an infection be identified before it occurs? It may be able to be predicted, but it can't be identified until it exists.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 8, 10-14, 16, 17, 21-27, 32-36, 38, 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over CDC plan 1998, in view of Frothingham (1998).

The claims are drawn to methods of tracking the spread of infectious bacteria. The methods comprise obtaining samples, sequencing VNTR's of the samples and storing the data, comparing the data with other sample data, identifying contaminated samples and tracking the spread. The methods can provide an unspecified "warning"; this is being broadly interpreted as providing a positive or negative result.

CDC Plan "Preventing Emerging Infectious Diseases; a strategy for the 21st Century, October, 1998" discloses methods of tracking and controlling infectious diseases. The document discloses Surveillance, and Response, Prevention and Control. Diseases of varying types including infectious diseases, foodborne diseases, airborne and zoonotic diseases, and diseases of travelers are all discussed. The Centers for Disease Control is an agency comprised of many elements, such as the National Center for Infectious Disease which can process patient samples and provide data. The CDC is linked to state and local health departments (which can obtain samples) comprising medical professionals, and to research facilities which comprise scientific personnel. Page 14 of the disclosure is a summary of the CDC plan. Surveillance is defined as "the ongoing systematic collection, analysis interpretation and dissemination of health data... Epidemiologists use these data to detect outbreaks; characterize disease transmission patterns by time, place and person; evaluate prevention and control programs and project future health care needs." (page 17). The collection of samples meets step (1) of the method. The analysis and interpretation encompasses steps (2-4) of the method. Detecting the outbreak and characterization meet the limitations of steps (5 and 6) and the dissemination meets the "warning" step of the claimed method. The FoodNet is an illustration of a system with a

centralized database which performs the disclosed method. The FoodNet collects data obtained from patient specimens, compares and tracks the data. The FoodNet can provide warnings as to infection spread or outbreak. EMERGEncyIDNET , IDSA EIN, WHO Polio Lab Network, and GeoSentinel are other networked systems for tracking and controlling infections. The patient specimens can be obtained from Emergency departments, Infectious Disease Practicioners, and Clinics. Objects (food) and Object locations (place of manufacture, or sale, or consumption) as well as patient locations can all be tested and/or tracked. Issues of patient confidentiality are discussed. Samples are compared against local and international data. Warnings are specifically noted in the GeoSentinel summary as "travel advisories".

The CDC Plan specifically indicates that molecular fingerprinting techniques are to be used to distinguish between strains or isolates of bacteria, fungi viruses or parasites. M. tuberculosis is a specifically contemplated infection. Methods used include comparing sequences and comparing the sizes of fragments. These tests are to be performed on patient samples, as well as objects and/or locations such as water supplies, food shipments, infected animals, etc. This plan creates a "real-time, on-line" capacity to identify and compare certain strains of bacteria. Particular subsystems specified by this plan include geographic information systems and computer programs that detect subtle variations of surveillance data that may indicate disease outbreaks. Early Warning systems are also disclosed to disseminate information on a wide scale.

At page 27, the plan specifically encourages the development of new diagnostic testing methods. The creation of tools for the collection and analysis of risk factor data, geographic information systems and remote sensing technologies and specifically disclosed.

The CDC Plan does not disclose the sequencing of the VNTR (Variable Number of Tandem Repeats) regions of the bacteria in the samples.

Frothingham et al. (1998, PTO-1449) discloses methods of assessing genetic diversity of a pathogen through the sequencing of the VNTR region of the pathogen. Frothingham et al. obtain patient samples and sequence the VNTR region of the pathogen M. Tuberculosis. Primers are used to amplify the VNTR, then its size and sequence are determined. Comparison of the presence, size and sequence of these regions between samples provided a measure of diversity. Numbers of direct repeat sequences, the level of insertion or the level of deletion can be

determined. Multiple distinct strains were identified and discriminated. The methods were determined to be stable and reproducible. Frothingham specifically notes that this procedure can be used in strain differentiation for diagnosis of infection and evolutionary studies. Other considered uses are epidemiological investigation, identification of outbreak-related strains and recognition of cross contamination. This method is an improvement over prior diagnostic techniques such as molecular fingerprinting. The previous art recognized standard, the molecular fingerprinting test, for M Tuberculosis had poor discriminatory power.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the VNTR sequencing of Frothingham in the CDC Plan for controlling and tracking infection. One of skill in the art would have been motivated to incorporate the methods of Frothingham, as they were shown to be an improvement over known techniques. The improved discrimination between types of a pathogen allow for more specific identification of the etiology of an outbreak, and better tracking of specific related infections. The high level of one of skill in the art of microbiology and medicine indicate that the methods could have reasonably been performed. One of skill in the art would have had a reasonable expectation of success at combining the methods of Frothingham with the CDC Plan, as the CDC Plan specifically provides for the incorporation of new specific diagnostic testing. Therefore the entire invention, as a whole, would have been prima facie obvious, absent evidence to the contrary.

Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, 38 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over CDC plan 1998, in view of Van Belkum (1998).

Claim 7 specifies that the method tests for VNTR in the Protein A or coagulase genes of S Aureus. Claims 28-31 add multiple region sequencing.

CDC Plan "Preventing Emerging Infectious Diseases; a strategy for the 21st Century, October, 1998" discloses methods of tracking and controlling infectious diseases. The document discloses Surveillance, and Response, Prevention and Control. Diseases of varying types including infectious diseases, foodborne diseases, airborne and zoonotic diseases, and diseases of travelers are all discussed. The Centers for Disease Control is an agency comprised of many elements, such as the National Center for Infectious Disease which can process patient

samples and provide data. The CDC is linked to state and local health departments (which can obtain samples) comprising medical professionals, and to research facilities which comprise scientific personnel. Page 14 of the disclosure is a summary of the CDC plan. Surveillance is defined as "the ongoing systematic collection, analysis interpretation and dissemination of health data... Epidemiologists use these data to detect outbreaks; characterize disease transmission patterns by time, place and person; evaluate prevention and control programs and project future health care needs." (page 17). The collection of samples meets step (1) of the method. The analysis and interpretation encompasses steps (2-4) of the method. Detecting the outbreak and characterization meet the limitations of steps (5 and 6) and the dissemination meets the "warning" step of the claimed method. The FoodNet is an illustration of a system with a centralized database which performs the disclosed method. The FoodNet collects data obtained from patient specimens, compares and tracks the data. The FoodNet can provide warnings as to infection spread or outbreak. EMERGEncyIDNET , IDSA EIN, WHO Polio Lab Network, and GeoSentinel are other networked systems for tracking and controlling infections. The patient specimens can be obtained from Emergency departments, Infectious Disease Practicioners, and Clinics. Objects (food) and Object locations (place of manufacture, or sale, or consumption) as well as patient locations can all be tested and/or tracked. Issues of patient confidentiality are discussed. Samples are compared against local and international data. Warnings are specifically noted in the GeoSentinel summary as "travel advisories".

The CDC Plan specifically indicates that molecular fingerprinting techniques are to be used to distinguish between strains or isolates of bacteria, fungi viruses or parasites. S Aureus, and M tuberculosis are specifically contemplated infections. Methods used include comparing sequences and comparing the sizes of fragments. These tests are to be performed on patient samples, as well as objects and/or locations such as water supplies, food shipments, infected animals, etc. This plan creates a "real-time, on-line" capacity to identify and compare certain strains of bacteria. Particular subsystems specified by this plan include geographic information systems and computer programs that detect subtle variations of surveillance data that may indicate disease outbreaks. Early Warning systems are also disclosed to disseminate information on a wide scale.

At page 27, the plan specifically encourages the development of new diagnostic testing methods. The creation of tools for the collection and analysis of risk factor data, geographic information systems and remote sensing technologies and specifically disclosed.

The CDC Plan does not disclose the sequencing of the VNTR (Variable Number of Tandem Repeats) regions of the bacteria in the samples, or to perform this particular analysis onf the protein A or coagulase genes of S Aureus.

Van Belkum (SSR Loci in Prokaryotic Genomes; MMBR 1998 62:275-293: PTO 1449) discloses methods of assessing genetic diversity of a pathogen through the sequencing of the VNTR region of the pathogen. Van Belkum obtain patient samples and sequence the VNTR region of the protein A gene and/or coagulase gene of S Aureus. (see pages 283-284.). Primers can be used to amplify the VNTR, then its size and sequence are determined. Comparison of the presence, size and sequence of these regions between samples can provide a measure of diversity. Numbers of direct repeat sequences, the level of insertion or the level of deletion can be determined. Multiple distinct strains were identified and discriminated. The methods were determined to be stable and reproducible. Van Belkum specifically notes that this procedure can be used in strain differentiation for diagnosis of infection and evolutionary studies. The coagulase is a major phenotypic species determinant in S Aureus. Van Belkum notes that repeat elements enable bacteria to respond to diverse environmental factors, which appear to be related to pathogenesis, and these elements are extremely important in the study of adaptive behavior. Van Belkum note the successful use of PCR mediated SSR amplification, followed by size study and using sequencing for the pathogens of H influenzae and C albcans. These repeats lend themselves to the development of novel assays suited for strain identification and definition of strain relatedness.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have incorporated the repeat sequence region sequencing of Van Belkum in the CDC Plan for controlling and tracking infection. One of skill in the art would have been motivated to incorporate the methods of Van Belkum, as they were shown to be an improvement over known techniques. The improved discrimination between types of a pathogen allow for more specific identification of the etiology of an outbreak, and better tracking of specific related infections. The high level of one of skill in the art of microbiology and medicine indicate that

the methods could have reasonably been performed. One of skill in the art would have had a reasonable expectation of success at combining the methods of Van Belkum with the CDC Plan, as the CDC Plan specifically provides for the incorporation of new specific diagnostic testing. Therefore the entire invention, as a whole, would have been prima facie obvious, absent evidence to the contrary.

Conclusion

No claim is allowed. **This action is non-final.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Mary K Zeman** whose telephone number is (571) 272 0723

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD can be reached on (571) 272 0718. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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3/10/06